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UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
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HEALTH EFFECTS DIVISION
SCIENTIFIC DATA REVIEWS
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OFFICE OF
PREVENTION, PESTICIDES
AND TOXIC SUBSTANCES

Date: 7/22/08

Subject: Myclobutanil. Amended Human-Health Risk Assessment for Proposed Use on Section 3 Requests for Use on Snap Bean, Mint, Papaya, Gooseberry, Currant, Caneberry, Bell and Non-Bell Pepper, Head and Leaf Lettuce, and Artichoke.

PC Code: 128857	DP Barcode: 354903 (341689)
Decision No.: 372360	Registration No.: 62719-411, 62719-411
Petition No.: 7E4861, 7E4877, 3E6562, 8E4939, 6E7138, & 7E4866	Regulatory Action: Section 3
Risk Assessment Type: Single	Case No.: NA
TXR No.: NA	CAS No.: 88671-89-0
MRID No.: NA	40 CFR: 443

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INTRODUCTION

The ARIA Team of the Office of Pesticide Programs (OPP) is charged with estimating the risk to human health from exposure to pesticides. The RD of OPP has requested that ARIA update the latest human health risk assessment for the pesticide myclobutanil [α-butyl-α-(4-chlorophenyl)-1*H*-1,2,4-triazole-1-propanenitrile] (PP#s: 7E4861, 7E4877, 3E6562, 8E4939, 6E7138, & 7E4866. DP Num: 341689, W. Cutchin, 11/1/07) to include updated information for the determination of the Safety Factor for infants and children. No other changes are required.

Rcvd in RAC 7/24/2008 EW

4.0 Food Quality Protection Act (FQPA) Assessment

In general. Section 408 of FFDCA provides that EPA shall apply an additional (``10X") tenfold margin of safety for infants and children in the case of threshold effects to account for prenatal and postnatal toxicity and the completeness of the database on toxicity and exposure unless EPA determines based on reliable data that a different margin of safety will be safe for infants and children. This additional margin of safety is commonly referred to as the FQPA safety factor. In applying this provision, EPA either retains the default value of 10X when reliable data do not support the choice of a different factor, or, if reliable data are available, EPA uses a different additional FQPA safety factor value based on the use of traditional UFs and/or special FQPA safety factors, as appropriate.

Prenatal and postnatal sensitivity. There is no indication of quantitative or qualitative increased susceptibility in rats or rabbits from *in utero* and/or postnatal exposure to myclobutanil. In the rat developmental toxicity study, maternal toxicity, which included rough hair coat and salivation, alopecia, desquamation and red exudate around the mouth occurs at the same dose level as increases in incidences of 14th rudimentary and 7th cervical ribs in the fetuses. The maternal and developmental toxicity NOAELs in the rat developmental toxicity study were 93.8 mg/kg/day. EPA concludes that there is no evidence qualitative susceptibility in rat developmental toxicity study since the fetal variations (14th rudimentary ribs and 7th cervical ribs) are normal occurance control animals that occurred in the presence of severe maternal toxicity (red exudate around mouth and salivation). In the rabbit developmental toxicity study there is reduced body weight and body weight gain during the dosing period, clinical signs of toxicity such as bloody urine and bloody urogenital or anal area and a possible increase in abortions (blood and/or aborted material in the cage pan) in the does at the same dose level as developmental toxicity manifested as increased resorptions, decreased litter size and decreased viability index. The maternal and developmental toxicity NOAELs in the rabbit developmental toxicity study were 93.8 mg/kg/day. EPA concludes that there is no evidence qualitative susceptibility in rabbit developmental toxicity study since the fetal effects (resorptions, decreased litter size and viability) occurred in the presence of equally severe maternal toxicity (abortions, bloody urine and bloody urogenital or anal area). The maternal NOAEL in the 2-generation reproduction study was 50 ppm (2.5 mg/kg/day) based on hepatocellular hypertrophy and increased liver weight seen at 200 ppm (10 mg/kg/day; LOAEL). The offspring toxicity NOAEL was 200 ppm (10 mg/kg/day) based on decreased pup body weight gain during lactation seen at 1,000 ppm (50 mg/kg/day; LOAEL). The reproductive toxicity NOAEL was 200 ppm (10 mg/kg/day) based on increased incidences in the number of still born pups and atrophy of the testes, epididymides and prostate observed at 1,000 ppm (50 mg/kg/day; LOAEL). EPA concludes that there is no evidence on increased susceptibility (qualitative or quantitative) in the 2-generation reproduction study in rats because the offspring and reproductive toxicity were observed at a higher dose than the dose that caused maternal toxicity.

EPA has determined that reliable data show that it would be safe for infants and children to reduce the FQPA safety factor to 1X. That decision is based on the following findings:

i. The toxicity database for myclobutanil is complete.

ii. There is no indication that myclobutanil is a neurotoxic chemical and there is no need for a developmental neurotoxicity study or additional UFs to account for neurotoxicity.

iii. There is no evidence that myclobutanil results in increased susceptibility in in utero rats or rabbits in the prenatal developmental studies or in young rats in the 2-generation reproduction study.

iv. There are no residual uncertainties identified in the exposure databases. The acute dietary food exposure assessment (females 13 to 49 years old only) utilizes existing and proposed tolerance level residues and 100 PCT information for all commodities. The chronic dietary food exposure assessment utilizes existing and proposed tolerance level residues; USDA Pesticide Data Program (PDP) monitoring data for apple juice, bananas (not plantains) and milk; average PCT data for some commodities and 100 PCT information for all other commodities. The dietary drinking water assessment utilizes water concentration values generated by model and associated modeling parameters, which are designed to provide conservative, health protective, high-end estimates of water concentrations which will not likely be exceeded.

v. The residential handler assessment is based upon the residential standard operating procedures (SOPs) and utilized unit exposure data from the Outdoor Residential Exposure Task Force (ORETF) and the Pesticide Handler's Exposure Database (PHED). The residential post-application assessment is based upon chemical-specific turf transferable residue (TTR) data and DFR data. The chemical-specific study data as well as the surrogate study data used are reliable and also are not expected to underestimate risk to adults as well as to children. In a few cases where chemical-specific data were not available, the SOPs were used alone. The residential SOPs are based upon reasonable ``worst-case" assumptions and are not expected to underestimate risk.

These assessments of exposure are not likely to underestimate the exposure to myclobutanil.

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